Remarks

Reconsideration of this Application is respectfully requested.

Claims 41, and 52-62 are pending in the application, with claim 41 being the independent claim. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph, Written Description

Claims 52, 55, 57, 58, 61 and 62 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. (Office Action, page 2.)

The test for the written description requirement is whether one skilled in the art can reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); MPEP § 2163.02. The Federal Circuit has re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed.'" *Union Oil of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). Furthermore, an applicant is not required to explicitly describe the subject matter. *Unocal*, 208 F.3d at 1000; *see also* MPEP § 2163.02 ("The subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba* in order for the disclosure to satisfy the description requirement.").

(1) The Examiner has alleged that there is no support in the specification as originally filed for the composition of claim 52 and that the specification does not disclose the "scope of claim 52 which encompasses other types of composition containing nonpharmaceutically acceptable carriers." (Office Action, page 2.) Applicants respectfully traverse the rejection.

Applicants again note that the Federal Circuit stated in *Univ. of Calif. v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), that:

> A description of a genus of cDNAs may be achieved by means of a recitation of [1] a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or [2] of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus . . . We will not speculate in what other ways a broad genus of genetic material may be properly described . . .

Univ. of Cal., 43 U.S.P.Q.2d at 1406. Thus, the Federal Circuit has stated that the written description requirement for a claim directed to a genus of molecules may be satisfied by providing the sequences of a *representative number of molecules which fall within the scope of the genus*. *See id* (emphasis added).

The Examiner has reiterated his statement that "the cited passage of the specification refers to vaccines and carriers for vaccines that constitute pharmaceutical carriers. The specification does not disclose the scope of claim 52 which encompasses other types of compositions containing nonpharmaceutically acceptable carriers." (Office Action, page 2.) Applicants again assert that a representative number of carriers have been described in the specification. Applicants have described several types of useful carriers which are known in the art, *e.g.*, thyroglobulin, albumins such as human

serum albumin, tetanus toxoid, polyamino acids such as poly L-lysine, poly L-glutamic acid, influenza, hepatitis B virus core protein and the like. (*See* Specification, page 43, lines 1-4.)

Thus, Applicants have described a representative number of different carriers within the general category of the genus "carrier." In view of the standard for written description described above, Applicants assert that they are in possession of the claimed invention and that "a composition comprising the peptide of claim 41 and a carrier" is clearly supported in the specification such that one of skill in the art would have reasonably concluded that the inventor, at the time the application was filed, had possession of the invention as recited in claim 52.

Regarding the term "nonpharmaceutically acceptable carrier," the Examiner alleges that Applicants had attributed a particular meaning to his term, *i.e.*, that "'nonpharmaceutically acceptable carriers' means carriers that are not pharmaceutically acceptable." (Office Action, page 2.) This is not, in fact, what Applicants had indicated in the last Office Action. Rather, Applicants had specifically noted that the specification describing examples of carriers is sufficient to describe "carrier" as recited in claim 52. Furthermore, Applicants had pointed out that it was particularly unclear what the Examiner meant by the term "nonpharmaceutically acceptable carrier." Specifically, Applicants stated the following:

> Furthermore, it is unclear what the Examiner means by the term "nonpharmaceutically acceptable carrier." For example, water or saline solution are sometimes considered nonpharmaceutically acceptable carriers (depending on the active ingredient and method of administration), but sometimes these may also be considered as "pharmaceutically acceptable" carriers. Considering water or saline solution as examples of nonpharmaceutically

> acceptable carriers, Applicants assert that these types of carriers were well known to one of ordinary skill in the art at the time of the filing of the present invention.

(Reply to Office Action, filed January 28, 2008, page 7.)

Thus, Applicants had stated that even assuming that water or saline solution were examples of a nonpharmaceutically acceptable carrier (the Examiner not having clarified the term), that these would be known to one of ordinary skill in the art, and would not necessarily have to be spelled out in the specification. Applicants had emphasized, however, that water or saline solution aside, the examples of carriers in the specification are examples of carriers in general, and thus the scope of claim 52 is supported.

(2) The Examiner has also reiterated that there is no support in the specification for the recitation of "wherein said one or more second peptides is a cytotoxic T cell (CTL)- inducing peptide or a helper T cell (HTL)-inducing peptide" in claim 55. (Office Action, page 4.) Applicants respectfully disagree. This description supports the concept that multiple peptide epitopes, CTL and/or HTL, can be combined into a single composition. In addition, the specification also discloses that

> [A] polyepitopic peptide composition comprising multiple CTL and HTL epitopes that target greater than 98% of the population may be created for administration to individuals at risk for both HBV and HIV infection. The composition can be provided as a single polypeptide that incorporates the multiple epitopes from the various diseases-associated sources, *or can be administered as a composition comprising one or more discrete epitopes.*

(Specification, page 84, lines 27-32) (emphasis added). Thus, the specification clearly contemplates that a second epitope, as recited in claim 55, can be a discrete CTL or HTL

epitope. Thus, a second epitope corresponding to either a CTL or HTL peptide is fully supported by the specification.

The Examiner then presents a similar argument as above regarding carriers. In particular, it is noted that "whilst the cited passages disclose vaccine compositions containing the components under consideration, the instant claims encompass nonvaccine compositions containing the aforementioned ingredients that are not disclosed in the specification." (Office Action, page 4.) Applicants point out that the CTL and HTL epitopes, as described in the specification, are representative examples of CTL and HTL epitopes in general. Thus, the scope of the claims is supported.

(3) The Examiner has again alleged that "[t]here is no support in the specification as originally filed for the composition of claims 61, 62." (Office Action, page 4.) In particular, the Examiner again reiterates that the specification "discloses the peptide of claim 61/62 linked to a CTL epitope . . . but does not disclose the claimed composition which is not a vaccine and wherein the peptides are not linked." (*Id.*) Applicants point out, as discussed above, that while the specification does describe embodiments where the CTL and/or HTL peptides of the invention are linked, that the specification also contrasts compositions where the peptides are provided together as a single polypeptide with compositions that "can be administered as a composition comprising one or more *discrete* epitopes." (Specification, page 84, lines 27-32 (emphasis added).) Previously, Applicants argued that in contrast to the Examiner's allegation, the specification provides support for compositions where the CTL and/or HTL peptides of the invention are both linked or unlinked. Additionally, the different pharmaceutical or vaccine compositions described in the specification are examples of compositions according to the invention.

Thus, the description of the different types of compositions fully support a composition according to claim 61 or 62.

With respect to HTL epitopes, the Examiner has stated that the cited passage refers to "'epitopes from the various disease associated sources' wherein the HTL peptides recited in the instant claims are not disease associated HTL." (Office Action, page 4.) As an initial matter, Applicants point out that, in addition to disease associated HTL, the specification also describes other types of HTLs including "loosely restricted HLA-restricted" or "promiscuous" HTLs. (*See e.g.*, page 50, line 28 to page 51, line 12). Representative examples of such "promiscuous" HTLs are also disclosed. (*See id.*) Applicants also point out that HTL as recited, for example, in claim 55, does in fact encompasses disease associated HTL. Thus, any disease associated HTL described in the specification is a representative example of an HTL according to the claims. Thus, the scope of the claims is supported.

(4) The Examiner has further reiterated the rejection of claim 61 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement because the "claims encompass a vast collection of artificial peptides with the functional attributes of a pan-DR binding epitope wherein the identity of said peptides is not disclosed in the specification and it appears unpredictable as to what peptides would or would have said functional attributes." (Office Action, page 5.) As previously noted, contrary to the Examiner's assertion, Applicants point out that the specification describes pan-DR binding epitopes, and not just "a single peptide with said attributes" as the Examiner suggests. Specifically, Applicants disclose the following:

> In certain embodiments, the T helper peptide is one that is recognized by T helper cells present in the majority of the

> populations. This can be accomplished by selecting amino acid sequences that bind to many, most, or all of the HLA class II molecules. These are known as "loosely HLA-restricted" or "promiscuous" T helper sequences. Examples of amino acid sequences that are promiscuous include sequences from antigens such as tetanus toxoid at positions 830-843 (QYIKANSKFIGITE), *Plasmodium falciparum* CS protein at positions 378-398 (DIEKKIAKMEKASSVFNVVNS), and Streptococcus 18kD protein at positions 116 (GAVDSILGGVATYGAA). Other examples include peptides bearing a DR 1-4-7 supermotif, or either of the DR3 motifs.

(Specification, page 50, line 28 to page 51, line 2.) Thus, the specification not only describes the functional attributes of a pan-DR binding epitope, but also provides several examples of well-known and frequently-utilized pan-DR binding epitopes. In view of the above, one of ordinary skill in the art would readily and predictably understand what is meant by the term "pan-DR binding epitope."

Furthermore, "[t]he 'written description' requirement must be applied in the context of the particular invention and the state of knowledge." *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005). "Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter." *Id.* at 1359. Applicants assert that in view of the description in the specification discussed above, and in view of the existing knowledge in the particular field of the invention, one of ordinary skill in the art would understand what is meant by the term "pan-DR binding epitope" in the context of the present invention.

In view of the discussion above, Applicants therefore assert that claims 52, 55, 57, 58, 61 and 62 satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully assert that the Examiner withdraw the rejection.

Rejection under 35 U.S.C. § 112, first paragraph, Enablement

Claims 53 and 58 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. (Office Action, page 7.)

Specifically, the Examiner reasserts the same statement as set forth in the previous substantive Office Action that "the specification does not disclose how to use the instant invention for the in vivo treatment/prevention of HBV in humans." (*Id.*) Applicants again disagree and respectfully traverse the rejection.

In order for a claim to be enabled, the specification must teach one of ordinary skill in the art to make and use the invention without undue experimentation. The factors that can be considered in determining whether an amount of experimentation is undue have been set forth in *In re Wands*, 858 F.2d731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: 1) the guidance provided by the specification; 2) the amount of pertinent literature; 3) the presence of working examples; and 4) the predictability of the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *See id.*

As Applicants have noted previously, the Examiner's rejection is one based on "how to use." Applicants again respectfully remind the Examiner that

> [W]hen a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire score of that claim is sufficient to preclude a rejection for nonenablement based on how to use . . . if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.

M.P.E.P. § 2164.01(c).

The Examiner again reiterates the same argument stating that "the claimed inventions are drawn to a pharmaceutical composition that can be used to treat/prevent HBV infection. The substantial/real life use for the claimed inventions are preventing and treating HBV infection in humans." (Office Action, page 8.) However, the Examiner's comments again do not address Applicants' argument that there is *no use limitation recited in the claims*. The Examiner simply again states that there is an intended use limitation when, in fact, there is not. Applicants again assert that the instant claims are not limited by a recited use, so any enabled use disclosed in the specification enables the claims if the use is in keeping with their scope.

"As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims." MPEP § 2164.08 (2006) (citing *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003); *In re Moore*, 439 F.2d 1232, 1236 (C.C.P.A. 1971); *see also Plant Genetic Sys., N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339 (Fed. Cir. 2003).

Without disclaiming or disparaging any of the uses disclosed by the specification, Applicants again note that the enablement requirement does not require data showing treatment efficacy or any clinical use as it would appear that the Examiner would require.

Applicants assert that the "pharmaceutical composition" of claim 53 or 58 is simply one which contains the claimed peptides as well as, for example, pharmaceutically-acceptable excipients. This composition can be used, for example, to assay the activity of peptides in transgenic mice as described in Example 8 of the specification. Thus, Applicants have enabled the claimed invention for at least one use which correlates with the claimed invention.

"[A] specification disclosure which contains a teaching of the manner and process of making and using the invention . . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support." *Rasmusson v. Smithkline Beecham Corp.*, 413 F.3d 1318, 1323 (Fed. Cir. 2005) (quoting *In re Marzocchi*, 439 F.2d 220, 223 (C.C.P.A. 1971)). As discussed above, the application as filed provides an enabling disclosure of the presently claimed composition.

The Examiner again reiterates that for the claimed invention to be enabled, Applicants must demonstrate the clinical efficacy of the claimed composition. Applicants again assert that there is no requirement for clinical data to prove that an application is in compliance with 35 U.S.C. § 112, first paragraph. In fact, description of *in vitro* and/or animal testing has been held to enable claims to *in vivo* therapeutic compositions and methods of their use. To this end, the Federal Circuit has stated that:

> In vitro testing, in general, is relatively less complex, less time consuming, and less expensive than in vivo testing. Moreover, in vitro results with respect to the particular pharmacological activity are generally predictive of in vivo test results, i.e., there is a reasonable correlation

> therebetween. Were this not so, the testing procedures of the pharmaceutical industry would not be as they are.

Cross v. Iizuka, 753 F.2d 1040, 1050 (Fed. Cir. 1985); *see also In re Brana*, 51 F.3d 1560, 1567-68 (Fed. Cir. 1995) (holding that animal testing results are sufficient to establish whether one skilled in the art would believe that a pharmaceutical compound has an asserted clinical utility for the purposes of compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph). Thus, even assuming that Applicants would have to enable an artificially created use limitation recited in the claims, Applicants note that the specification provides *in vitro*, as well as *in vivo* assays, as to how the peptides and compositions of the invention would be assayed, for example, for their immunogenicity using animals.

In view of the foregoing discussion, Applicants submit that a person having ordinary skill in the art, in view of the teachings of the specification and the knowledge in the art, would be able to make and practice the full scope of Applicants' claimed invention. Accordingly, Applicants respectfully request that this rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Interpretation of Claim 41

The Examiner has stated "[i]n view of previously pending claim 45, claim 41 is interpreted as encompassing the peptide recited in the claim attached to another peptide(s)." (Office Action, page 10.) Applicants point out that claim 45 is no longer pending. Applicants note that claim 41 is directed to "[a]n isolated peptide less than 15 amino acids in length comprising an oligopeptide selected from the group consisting of: QAFTFSPTYK (SEQ ID NO:638); LVVDFSQFSR (SEQ ID NO:620); NVSIPWTHK

(SEQ ID NO:625); and SAICSVVRR (SEQ ID NO:653)." With regard to the presently claimed invention, Applicants do not intend for the peptide as recited in claim 41, to be attached to another peptide.

Rejection under 35 U.S.C. § 102

Claims 41, 52, 53, 55, 57, and 58 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Seeger *et al.* (Seeger), U.S. Patent No. 5,360,714, as evidenced by Pasek *et al.* (Pasek). (Office Action, page 12.) Applicants respectfully disagree and traverse the rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); MPEP § 2131. Seeger fails to teach every aspect of the claimed invention.

Applicants note that independent claim 41 is directed to an isolated peptide *less than 15 amino acids in length*. Seeger does not disclose the exact peptide as recited in claim 41. Seeger only discloses a peptide sequence that *comprises* Applicants' claimed peptide. (*See* Seeger, col. 10, 3rd paragraph, col. 5, 3rd paragraph, cols 11-12.)

With respect to dependent claims 52, 53, 55, 57, and 58, Applicants note that "[t]he standard for lack of novelty under 35 U.S.C. §102, that is, for 'anticipation,' is one of strict identity." *See* Chisum, Donald S., *Chisum on Patents*, 1:3.02[1], Matthew Bender & Co., Inc. (2002). To anticipate a claim, a single source of prior art must disclose all of the limitations (sometimes called elements) of the claim. *See id.* As stated by the Federal Circuit in *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558,

1566 (Fed. Cir. 1996): "[t]o anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter." The absence of any claimed element from the reference negates anticipation. *Minn. Mining & Mfg.*, 976 F.2d at 1572 (*citing Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1574 (Fed. Cir. 1984)).

Dependent claims 52, 53, 55, 57, and 58 depend, either directly or indirectly, from claim 41, and therefore incorporate all of the limitations of claim 41. *See* 35 U.S.C. § 112, fourth paragraph. As discussed above, Seeger does not disclose the exact peptide as recited in the claim 41. Dependent claims 52, 53, 55, 57, and 58 incorporate the limitations of claim 41, and therefore, Seeger also does not disclose all of the limitations of claims 52, 53, 55, 57, and 58.

As to § 102 anticipation rejections, if an independent claim is not fully met by an alleged prior art reference, neither are the more limited dependent claims. *See Application of Royka,* 490 F.2d 981, 983-984 (Cust. & Pat. App. 1974). "It is elementary that to support an anticipation rejection, all elements of the claim must be found in the reference." Indeed, in *Royka*, the Board found that "[t]he dependent claims rejected with [independent] claim 28, as anticipated under § 102, are not anticipated since [independent] claim 28 is not anticipated." *Id.*

Seeger does not disclose the peptide recited in claim 41, nor does it additionally disclose the further limitations of claims 52, 53, 55, 57, and 58.

Thus, for at least the reasons discussed above, Applicants assert that Seeger does not teach all of the limitations of claims 41, 52, 53, 55, 57, and 58. Consequently,

Seeger does not anticipate these claims. As such, Applicants respectfully request that the rejection of these claims under 35 U.S.C. § 102(e) be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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